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EXAMINER	
HUYNH, PHUONG N	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/02/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/049,663	KIM ET AL.	
	Examiner	Art Unit	
	Phuong Huynh	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *8-17* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/15/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-18 are pending.

2. Applicant's election with traverse of Group 1, Claims 1-7 (now claims 1-7 and 18) drawn to a method for treating autoimmune rheumatoid arthritis, filed 3/29/04, is acknowledged. The traversal is on the grounds that a composition and a method of using that composition be examined together should the examiner not find a special technical feature shared by all the claims that make a contribution over the prior art. This is not found persuasive because of the reasons set forth in the restriction mailed 1/30/04. The inventions listed as Groups 1-15 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Nakaoka *et al* (Vaccine 14(13): 1251-56, 1996; PTO 892) teach a pharmaceutical composition comprising biodegradable polymers such as poly(DL-lactic acid) entrapping with an antigen such as ovalbumin and a pharmaceutical acceptable carrier such as phosphate-buffered saline solution (See entire document, page 1252, col. 2, second paragraph, in particular). Claim 17 differs from the teaching of the reference only that the pharmaceutical composition wherein the antigen is autoimmune antigen in an amount effective to induce tolerance against autoimmune response. The 5,681,571 patent (Oct 1997; PTO 892) teaches pharmaceutical compositions and method of treating autoimmune diseases such as autoimmune rheumatoid arthritis, uveoretinitis, EAE, and insulin dependent diabetes mellitus by induction of tolerance to specific autoantigen (See entire document, col. 3, lines 1-61, claims of '571 patent, in particular). The reference method comprises orally administering to a mammal such as mice (col. 9, line 18, in particular) or rat (see col. 3, line 18, in particular) autoantigen particulates such as collagen type II linked to a carrier such as CTB and LTB that binds to mucosa (See col. 8, lines 62-67, col. 3, line 16-17, in particular). The reference autoimmune disease such as rheumatoid arthritis, uveoretinitis, EAE, and insulin dependent diabetes mellitus are chronic T cell mediated autoimmune diseases that react with antigen of one's own tissues (See col. 1, line 26-28, in particular). It would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the ovalbumin in the pharmaceutical composition comprising biodegradable polymers such as poly(DL-lactic acid) entrapping with an antigen as taught by the Nakaoka *et al* for the autoimmune antigen such as collagen type II as taught by the '571 patent for a pharmaceutical

composition comprising biodegradable polymers such as poly(DL-lactic acid) entrapping with collagen type II to induce tolerance as taught by the '571 patent and Nakaoka *et al.*

Since Applicant's inventions do not contribute a special technical feature when viewed over the prior art they do not have single general inventive concept and lack unity of invention.

Accordingly, Groups 1-15 are not so linked as to form a single general inventive concept and restriction is proper. Therefore, the requirement of Group I (now claims 1-7 and 18) and Groups 2-15 is still deemed proper and is therefore made FINAL.

3. Claims 8-17 are withdrawn from further consideration by the examiner, 37 C.F.R. 1.142(b) as being drawn to non-elected inventions.

4. Claims 1-7 and 18 are being acted upon in this Office Action.

5. Claim 18 is objected to as the claim encompass non-elected embodiments.

6. Claim 2 is objected to because "poly(DL-lactide-co-glycolide)" should have been poly(D, L-lactide-co-glycolide).

7. The disclosure is objected to because of the following informality "poly(DL-lactide-co-glycolide)" on page 6, line 3 and on page 10, line 18, should have been poly(D, L-lactide-co-glycolide). Appropriate action is required.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-7, and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for a method of treating autoimmune arthritis which comprises administering orally to a subject suffering from autoimmune rheumatoid arthritis biodegradable poly (D, L-lactic acid) particles of approximately 300nm in diameter, or poly (D,L-lactic acid) particles entrapped with autoimmune peptide selected from the group consisting of SEQ ID NO: 1-4, **does not** reasonably provide enablement for (1) a method for treating *all* autoimmune

diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers of any size in an effective amount to induce tolerance against all autoimmune response, (2) the said method wherein said biodegradable polymers are any poly(DL-lactide-co-glycolide), any polylactides or polyglycolides of any size, (3) the said method wherein said mammal is human, rats, mice, and monkeys, (4) the method for treating *all* autoimmune diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers in an effective amount to induce tolerance against all autoimmune response, wherein a single dose of any particles are mentioned above is administered to induce tolerance against any autoimmune response, (5) the method for treating *all* autoimmune diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers in an effective amount to induce tolerance against all autoimmune response, wherein the particles have a size of less than about 500 nm. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient

to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only a method of treating a specific autoimmune disease via inducing oral tolerance by administering orally particles of biodegradable polymers poly (D,L-lactide-co-glycolide) of approximately 300nm in diameter alone or entrapped with the specific autoimmune antigen such as peptide consisting of SEQ ID NO: 1-4 for rheumatoid arthritis, peptide consisting of SEQ ID NO: 5-9 for multiple sclerosis, peptide consisting of SEQ ID NO: 10 for autoimmune uveitis and peptide consisting of SEQ ID NO: 11 for IDDM using the appropriate animal model. The specification further discloses that mice fed with poly (D,L-lactide-co-glycolide) of approximately 300nm in diameter (PLGA) tend to have lower levels of T cell proliferative response to CII compared to collagen II fed mice (Figure 8(a) and 8(b). However, the level of IgG is not statistically different from mice with acetic acid (control) and the mean arthritis index of PLGA alone is not statistically different from acetic acid control (Fig 7b). Further, the specification discloses term "particle(s)" include both the polymer particles and the antigen-entrapping polymer particles (See page 10, line 1-3 of specification).

The specification does not teach how to make particles of biodegradable polymers of any size or any particles entrapped with any autoimmune antigen because there is insufficient guidance as to the structure and function of any particles, and autoimmune antigen without the amino acid sequence, let alone treating all autoimmune diseases.

Matsunaga *et al* teach that oral administration of autoantigen depends not only on the dose of antigen, but also the frequency and interval of administration, forms and metabolism of the antigen (See page 580, column 1, second and third paragraphs, in particular). Matsunaga *et al* further teach that the size of microspheres such as poly-D, L-lactic acid under 5μm were taken up into the PP and then translocated to the spleen, a systemic lymphoid tissue, which led to the production of anti-OVA specific IgG antibody. However, larger microspheres were not noticed in the spleen. In short, the size of the carrier bead or particle of biodegradable polymers regulates the nature of immune response elicited upon oral immunization.

Panyam *et al* teach particle size is an important parameter that could affect the degradation of the polymer matrix and formulation parameters include polymer and protein molecular weight, composition, formulation method, particular sized and the type of emulsifier used have important ramification for sustained delivery of therapeutic agents (See page 174, in particular). Given the indefinite number of particles biodegradable polymers, formulation,

particle sizes, it is unpredictable which undisclosed particles biodegradable polymers are effective for treating all autoimmune diseases.

Even if the particles of biodegradable polymers is limited to poly (D, L-lactide-co-glycolide) of approximately 300 nm in diameter, there is insufficient in vivo working examples demonstrating that the claimed method could treat all autoimmune diseases using only the collagen induced rheumatoid arthritis as a model. Again, the mean arthritis index of PLGA alone is not statistically different from the acetic acid control (Fig 7b).

Given the indefinite number of autoimmune disease and the limited in vivo working example in the specification as filed, it is not clear that reliance of collagen induced rheumatoid arthritis model accurately reflects the efficacy of the claimed therapeutic strategy since autoimmune disease is model dependent as taught by Van Noort *et al.* Van Noort *et al* teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). It is unpredictable which undisclosed autoimmune disease such as any Th1 mediated or T cell mediated autoimmune diseases are treatable with the claimed method.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

10. Claims 1-7, and 18 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) a method for treating *all* autoimmune diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and

glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers in an effective amount to induce tolerance against all autoimmune response, (2) the said method wherein said biodegradable polymers are any poly(DL-lactide-co-glycolide), any polylactides or polyglycolides of any size, (3) the said method wherein said mammal is human, rats, mice, and monkeys, (4) the method for treating *all* autoimmune diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers in an effective amount to induce tolerance against all autoimmune response, wherein a single dose of any particles are mentioned above is administered to induce tolerance against any autoimmune response, (5) the method for treating *all* autoimmune diseases, any autoimmune disease such as any Th1-mediated or T cell mediated autoimmune diseases, rheumatoid arthritis, insulin dependent diabetes mellitus, uveitis, multiple sclerosis, autoimmune thyroiditis, autoimmune hepatitis, interstitial pneumonitis, and glomerulonephritis and any corresponding diseases in all animal models which comprises administering orally to all mammal suffering from any autoimmune diseases *any* particles of biodegradable polymers in an effective amount to induce tolerance against all autoimmune response, wherein the particles have a size of less than about 500 nm.

The specification discloses only a method of treating a specific autoimmune disease via inducing oral tolerance by administering orally particles of biodegradable polymers poly (D,L-lactide-co-glycolide) of approximately 300nm in diameter alone or entrapped with the specific autoimmune antigen such as peptide consisting of SEQ ID NO: 1-4 for rheumatoid arthritis, peptide consisting of SEQ ID NO: 5-9 for multiple sclerosis, peptide consisting of SEQ ID NO: 10 for autoimmune uveitis and peptide consisting of SEQ ID NO: 11 for IDDM using the appropriate animal model. The specification further discloses that mice fed with poly (D,L-lactide-co-glycolide) of approximately 300nm in diameter (PLGA) tend to have lower levels of T cell proliferative response to CII compared to collagen II fed mice (Figure 8(a) and 8(b). However, the level of IgG is not statistically different from mice with acetic acid (control) and the mean arthritis index of PLGA alone is not statistically different from PLGA entrapped with

collagen II (Fig 7a). The specification discloses term "particle(s)" include both the polymer particles and the antigen-entrapping polymer particles (See page 10, line 1-3 of specification).

With the exception of the specific particles of biodegradable polymers poly (D, L-lactide-co-glycolide) of approximately 300nm in diameter for treating collagen induced autoimmune rheumatoid arthritis using only the DBA1 mouse model, there is insufficient written description about the structure associated with function of any particles of biodegradable polymers in claim 1 without the chemical formula, the size of the particles in claim 2 for the claimed method of treating all autoimmune diseases. Further, the specification discloses only (D, L-lactide-co-glycolide) of approximately 300nm in diameter for treating only rheumatoid arthritis, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398; University of Rochester v. G.D. Searle & Co., 69 USPQ2d 1886 (CA FC2004).*

Applicant is directed to the Final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 103(a) that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. This application currently names joint inventors. In considering Patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

13. Claims 1-5 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over the US Pat No 5,681,571 (Oct 1997; PTO 892) in view of US Pat No 5,075,109 (Dec 1991; PTO 892).

The '571 patent teaches a method of treating autoimmune diseases such as autoimmune rheumatoid arthritis, uveoretinitis, EAE, and insulin dependent diabetes mellitus by induction of tolerance to specific autoantigen (See entire document, col. 3, lines 1-61, claims of '571 patent, in particular). The reference method comprises orally administering to a mammal such as mice (col. 9, line 18, in particular) or rat (see col. 3, line 18, in particular) autoantigen particulates such as collagen type II linked to a carrier such as CTB and LTB that binds to mucosa (See col. 8, lines 62-67, col. 3, line 16-17, in particular). The reference autoimmune disease such as rheumatoid arthritis, uveoretinitis, EAE, and insulin dependent diabetes mellitus are chronic T cell mediated autoimmune diseases that react with antigen of one's own tissues (See col. 1, line 26-28, in particular).

The invention in claim 1 differs from the teachings of the reference only in that the method of treating autoimmune disease comprises administering orally particles of biodegradable polymers instead of autoantigens particulates linked to carrier CTB or LTB.

The invention in claim 2 differs from the teachings of the reference only in that the method of treating autoimmune disease wherein the biodegradable polymers are poly(D, L-lactide-co-glycolide), polylactides or polyglycolides.

The '109 patent teaches a method of potentiating an immune response by orally administering carriers such as particles of biodegradable polymers poly(D, L-lactide-co-glycolide), polylactides or polyglycolides microspheres that targets to the Peyers' patch or GALT (See entire document, col. 3, lines 32-60, in particular). The reference method comprises administering orally the reference biodegradable polymers entrapped with the desired antigen, proteins (See col. 15, lines 55-58, in particular). The reference poly(D, L-lactide-co-glycolide) have a size of less than 1 μm to 10 micrometer (See col 13, line 55-56, in particular). The reference poly(D, L-lactide-co-glycolide) has adjuvant activity of equal magnitude to common laboratory protein carrier such as keyhole limpet hemocyanin (KLH) and carbohydrate antigens such as type 3 streptococcus pneumoniae (see col. 17 lines 65 bridging col. 18, claim 1 of '109 patent, in particular). The reference method is advantageous because orally immunization using the reference poly (D, L-lactide-co-glycolide) enhances immunity at the mucosa by targeting the antigen of interest to the Peyer's patch and appears to be of long duration (See col. 8, lines 45-60, in particular).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to substitute the carrier such as CTB or LTB in the method of treating autoimmune diseases as taught by the '571 patent for the carrier such as poly(D, L-lactide-co-glycolide), polylactides or polyglycolides microspheres as taught by the '109 patent. From the combined teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention.

One having ordinary skill in the art would have been motivated to do this because the '571 patent teaches carrier CTB or LTB binds to mucosa and has adjuvant activity to enhance the immunity of autoantigens (See col. 8, lines 62-67, col. 3, line 16-17, in particular). The '109 patent teaches carriers such as particles of biodegradable polymers poly(D, L-lactide-co-glycolide), polylactides or polyglycolides microspheres targets to the Peyers' patch or GALT (See entire document, col. 3, lines 32-60, in particular), has adjuvant activity of equal magnitude to common laboratory protein carrier such as keyhole limpet hemocyanin (KLH) and carbohydrate antigens such as type 3 streptococcus pneumoniae (see col. 17 lines 65 bridging col. 18, claim 1 of '109 patent, in particular) and is advantageous because it enhances immunity at the mucosa by targeting the antigen of interest to the Peyer's patch and appears to be of long duration (See col. 8, lines 45-60, in particular). Claim 1 and 2 are included in this rejection because the specification defines the term "particle(s)" include both the polymer particles and the antigen-entrapping polymer particles (See page 10, line 1-3 of specification).

14. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over the US Pat No 5,681,571 (Oct 1997; PTO 892) in view of US Pat No 5,075,109 (Dec 1991; PTO 892) as applied to claims 1-5 and 18 and further in view of Desai *et al* (Pharmaceutical Research 13(12): 1838-1845, 1996; PTO 892).

The combined teachings of the '571 patent, and the '109 patent, have been discussed supra.

The invention in claim 6 differs from the teachings of the reference only in that the method of treating autoimmune disease wherein a single dose of said particles is administered to induce tolerance against autoimmune response.

The invention in claim 7 differs from the teachings of the reference only in that the method of treating autoimmune disease wherein said particles have a size of less than about 500nm.

Desai *et al* teach the successful development of oral vaccine based depends on the efficiency of uptake of microparticles by the gastrointestinal lymphoidal tissue and gastroinstestinal uptakes of biodegradable polymers such as poly(D, L-lactide-co-glycolide) depends on the size of the particles, i.e. 100 nm, 500nm, 1μm and 10 μm (See entire document). The efficiency of uptakes of PLGA of less than about 500nm such as 100 nm or 200nm size particles was 15-250 fold higher compared to large size particles and the Peyer's patch tissue had 2-200 fold higher uptake of particles than the non-patch tissue (See abstract, page 1842, column 1, second paragraph, in particular). Desai *et al* teach biodegradable particulate carrier systems are of interest as a potential means for oral delivery to enhance drug absorption, improve bioavailability, targeting of therapeutic agents to particular organs and reduce toxicity and to improve tolerance (see page 1838, column 1, in particular). Claim 6 is included in this rejection because it is within the purview of one ordinary skill in the pharmaceutical art to administer a single dose of particles based on the improved bioavailability and sustained release formulation as taught by the Desai et al (See page 1842, Fig 3, page 1844, column 1, in particular).

15. No claim is allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phuong Huynh "NEON" whose telephone number is (571) 272-0846. The examiner can normally be reached Monday through Friday from 9:00 am to 5:30 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The IFW official Fax number is (703) 872-9306.

17. Any information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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~~May 31,~~ 2004
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